Palvella Therapeutics Announces Scientific Publication in Journal of Vascular Anomalies Highlighting the Infiltrative Growth and Therapeutic Challenges of Microcystic Lymphatic Malformations

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Review delineates differences in clinical strategies between microcystic and macrocystic lymphatic malformations to guide disease-specific clinical trial design and treatment approaches

Manuscript emphasizes the importance of early therapeutic intervention in children to help reduce the risk of more serious complications over time

Review supports the scientific rationale of QTORIN™ 3.9% rapamycin anhydrous gel as a potential targeted therapy for microcystic lymphatic malformations

WAYNE, Pa., March 30, 2026 (GLOBE NEWSWIRE) -- Palvella Therapeutics, Inc. (Palvella or "the Company") (Nasdaq: PVLA), a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapies to treat patients suffering from serious, rare skin diseases and vascular malformations for which there are no U.S. Food and Drug Administration (FDA)-approved therapies, today announced the publication of a comprehensive review article in the *Journal of Vascular Anomalies (JoVA)* titled "Microcystic and Macrocystic Lymphatic Malformations: Distinct Genetics and Clinical Strategies."

"Microcystic lymphatic malformations remain one of the most difficult-to-treat vascular anomalies and represent a substantial unmet medical need," said Maria Buethe, M.D., Ph.D., Chief of the Pediatric Dermatology Division at Rady Children's Hospital of Orange County (RCHOC)/University of California, Irvine, and senior author of the publication. "Unlike macrocystic lesions, which can often be managed with interventional approaches, microcystic disease is characterized by diffuse tissue involvement, resistance to existing therapies, and frequent post-treatment recurrence. These distinctions underscore that lymphatic malformations cannot be approached as a single disease. To achieve meaningful and lasting patient outcomes, future research and therapy development must target the unique biological drivers of each specific subtype."

The review article highlights fundamental clinical differences between microcystic and macrocystic lymphatic malformations (LMs), reinforcing the significant unmet need in microcystic disease, where there are no FDA-approved therapies and where subtype-specific clinical trial design and targeted pharmacologic approaches are warranted. The publication highlights the following key distinguishing features of microcystic and macrocystic LMs:

Feature	Microcystic LMs	Macrocystic LMs
Size of Cysts	Small, diffuse cysts (<2 cm in diameter)	Large, fluid-filled cysts (>2 cm in diameter)
Structure	Dense network of small cysts infiltrating surrounding tissues	Discrete, few larger, fluid-filled cysts. Well-defined cysts, often singular or clustered
Common Locations	Often found on the cutaneous tissue or oral cavity	Commonly located in the neck, axilla, or mediastinum. Usually deep internal location
Clinical Presentation	Persistent lymphorrhea, bleeding, red/dark vesicles and plaques on the skin, highly prone to infection (cellulitis)	Visible swelling, compressible masses, may fluctuate in size
Risk of Spontaneous Regression	No spontaneous regression	Spontaneous regression possible, particularly in the head and neck (cystic hygroma)
Diagnosis	Clinical diagnosis	Easier to detect with US, CT, or MRI
Prognosis	Chronic, progressive disease. Worsens with time	Lower risk of recurrence, especially after complete removal
Complications	Increased risk of infection and cellulitis	May become secondarily infected or compress surrounding organs
Common Management Approaches	No FDA-approved therapies; interventional approaches not as effective	Sclerotherapy, surgical resection, possible observation for regression
Response to Treatment	No effective treatments	May resolve with fewer interventions; often better response to sclerotherapy

The publication further supports the scientific rationale of QTORIN™ rapamycin, which recently achieved the primary endpoint in the Phase 3 SELVA trial with highly statistically significant results across all pre-specified primary, key secondary, and secondary endpoints. Additionally, QTORIN™ rapamycin was well-tolerated, with systemic levels of rapamycin below 2ng/mL for all timepoints measured.

“An urgent need exists for safe and effective FDA-approved therapies for microcystic lymphatic malformations,” said Jeff Martini, Ph.D., Chief Scientific Officer of Palvella. “This publication reinforces that current procedural approaches are often inadequate for microcystic disease. We believe this work further supports Palvella’s strategy of developing QTORIN™ rapamycin as a targeted topical therapy designed specifically for patients with microcystic lymphatic malformations.”

About Microcystic Lymphatic Malformations

Microcystic LMs are a rare, chronically debilitating genetic disease caused by dysregulation of the phosphatidylinositol 3-kinase (PI3K)/mammalian target of rapamycin (mTOR) pathway. The condition is characterized by malformed lymphatic vessels that protrude through the skin and persistently leak lymph fluid (lymphorrhea) and bleed, often leading to recurrent serious infections and cellulitis that can cause hospitalization. The natural history of microcystic LMs is persistent and progressive without spontaneous resolution, with symptoms generally worsening over time, including increases in the number and size of malformed vessels that lead to complications and lifetime morbidity. There are currently no FDA-approved treatments for the estimated more than 30,000 diagnosed patients with microcystic LMs in the United States.

About Palvella Therapeutics

Founded and led by rare disease biotech veterans, Palvella Therapeutics, Inc. (Nasdaq: PVLA) is a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapies to treat patients suffering from serious, rare skin diseases and vascular malformations for which there are no FDA-approved therapies. Palvella is developing a broad pipeline of product candidates based on its patented QTORIN™ platform, with an initial focus on serious, rare skin diseases and vascular malformations, many of which are lifelong in nature. Palvella’s lead product candidate, QTORIN™ 3.9% rapamycin anhydrous gel (QTORIN™ rapamycin), is currently being developed for the treatment of microcystic lymphatic malformations, cutaneous venous malformations, and clinically significant angiokeratomas. Palvella’s second product candidate, QTORIN™ pitavastatin, is currently being developed for the treatment of disseminated superficial actinic porokeratosis. For more information, please visit www.palvellatx.com or follow Palvella on LinkedIn or X (formerly known as Twitter).

QTORIN™ rapamycin and QTORIN™ pitavastatin are for investigational use only and neither has been approved by the FDA o by any other regulatory agency for any indication.

Forward-Looking Statements

This press release contains forward-looking statements (including within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended (Securities Act)). These statements may discuss goals, intentions, and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current beliefs of the management of Palvella, as well as assumptions made by, and information currently available to, the management of Palvella. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as “may,” “will,” “should,” “would,” “expect,” “anticipate,” “plan,” “likely,” “believe,” “estimate,” “project,” “intend,” and other similar expressions or the negative or plural of these words, or other similar expressions that are predictions or indicate future events or prospects, although not all forward-looking statements contain these words. Statements that are not historical facts are forward-looking statements. Forward-looking statements include, but are not limited to, statements regarding the expected timing of the presentation of data from clinical trials, Palvella’s clinical development plans and related anticipated development milestones, Palvella’s plans to pursue Breakthrough Therapy Designation, Palvella’s plans to meet with regulatory authorities, Palvella’s cash, financial resources and expected runway, Palvella’s expectations regarding its programs, including QTORIN™ rapamycin and QTORIN™ pitavastatin, and its research-stage opportunities, including its expected therapeutic potential and market opportunity. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation: the ability to raise additional capital to finance operations; the ability to advance product candidates through preclinical and clinical development; the ability to obtain regulatory approval for, and ultimately commercialize, Palvella’s product candidates, including QTORIN™ rapamycin and QTORIN™ pitavastatin; the outcome of early clinical trials for Palvella’s product candidates, including the ability of those trials to satisfy relevant governmental or regulatory requirements; the fact that data and results from clinical studies may not necessarily be indicative of future results; Palvella’s limited experience in designing clinical trials and lack of experience in conducting clinical trials; the ability to identify and pivot to other programs, product candidates, or indications that may be more profitable or successful than Palvella’s current product candidates; the substantial competition Palvella faces in discovering, developing, or commercializing products; the negative impacts of global events on operations, including ongoing and planned clinical trials and ongoing and planned preclinical studies; the ability to attract, hire, and retain skilled executive officers and employees; the ability of Palvella to protect its intellectual property and proprietary technologies; reliance on third parties, contract manufacturers, and contract research organizations; and the risks and uncertainties described in the filings made by Palvella with the Securities and Exchange Commission (SEC), including the annual report on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, filed with or furnished to the SEC and available at www.sec.gov. The events and circumstances reflected in our forward-looking statements may not be achieved or

occur, and actual results could differ materially from those projected in the forward-looking statements. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that Palvella may face. Except as required by applicable law, Palvella does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. This press release contains hyperlinks to information that is not deemed to be incorporated by reference into this press release.

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